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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

*32*

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

## Office Action Summary

Application No <b>08/950,542</b>	Applicant(s) <b>Bachovchin</b>
Examiner <b>David Lukton</b>	Group Art Unit <b>1653</b>



Responsive to communication(s) filed on Jan 26, 2001

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 35 C.D. 11, 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

### Disposition of Claim

Claim(s) 35-51 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
Claim(s) \_\_\_\_\_ is/are allowed.  
 Claim(s) 35-51 is/are rejected.  
Claim(s) \_\_\_\_\_ is/are objected to.  
Claims \_\_\_\_\_ are subject to restriction or election requirement.

### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some\* None of the CERTIFIED copies of the priority documents have been received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

### Attachment(s)

Notice of References Cited PTO-892

Information Disclosure Statement(s) PTO-1449 Paper No(s) \_\_\_\_\_

Interview Summary PTO-413

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Pursuant to the directives of paper No. 44 (filed 1/26/01), claims 35 and 42 have been amended. Claims 35-51 remain pending.

Applicants' arguments filed 1/26/01 have been considered and found not persuasive.

\*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have not enabled one to obtain the requisite isomer with a purity of 96% or greater. As asserted by applicants, the procedure on page 15, lines 3-11 does not work and leads to an erroneous conclusion. As for the procedure on page 21, only the L,L and L,D isomers are referred to. As explained by applicants, there are four different isomers:

*cis*-L-Ala-D-boroPro and *trans*-L-Ala-D-boroPro

*cis*-L-Ala-L-boroPro and *trans*-L-Ala-L-boroPro.

interconversion of one or more isomers to other isomers under certain circumstances not explained in the specification. Accordingly, one would have to "know" that (a) the procedure on page 15, lines 3+ must be ignored, and (b) the procedure on page 21 is incomplete, and could easily lead to erroneous results. It is not enough to say that this or that isomer comes of "first", when in fact the term "L,L" really refers, in hindsight to a mixture of *cis*-L,L and *trans*-L,L; similarly the term "L,D" really refers, in hindsight, to a mixture of *cis*-L,D and *trans*-L,D isomers. Thus, the specification does not enable one to "make and use" the claimed invention. Moreover, even if it were true that enablement exists for purifying the compounds *cis*-L-Ala-L-boroPro and *trans*-L-Ala-L-boroPro, the claims encompass an infinite number of compounds, of size ranging from two amino acids to 2 million, and of polarities that cover the entire spectrum of highly lipophilic to highly hydrophilic. Even if applicants could make the argument that the procedure is clear for this one compound (which it is not), the issue of the *cis* and *trans* isomers would have to be dealt with for many of the remaining compounds in the genus.

\*

Claims 35-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

boron exceeds 96%. However, there does not appear to be support for this number. Similarly, claims 37-39 recite stereochemical purities of 97%, 98% and 99% respectively. Again, there is no support for this in the specification.

A few preemptive comments are made. On p. 21, line 24, an isomeric purity of "99-6%" is recited. However, this contains a typographical error, and because of the hyphen, is not actually a number. Perhaps what was intended is 99.6%, but if so, none of the pending claims would be supported by this number. In addition to the foregoing, on page 15, line 7, it is stated that "the early fraction appears by NMR analysis to be 95% enriched in one isomer". Again, this does not support the quantity of 96% or 97% or 98% or 99%. But in addition, were applicants to amend the claims to recite a stereochemical purity of 95%, this ground of rejection would be maintained. That is because applicants have effectively argued that the paragraph encompassing lines 3-11 on page 15 should be completely disregarded because it includes an erroneous conclusion. Applicants have argued that *In re Wiggins*, together with their declaration, should effectively eliminate the teaching on page 3743, col 1, paragraph 3 of Bachovkin (*J. Biol. Chem.* **265**, 3738, 1990). As it happens, that particular paragraph contains the same information as the paragraph on page 15 (lines 3-11) of the specification. Accordingly, applicants cannot argue that, on the one hand, the procedure on page 15 (line 3+) must be ignored, but at the same time, that the

There is another issue which is somewhat related to the foregoing. Claims 35 and 42 make reference to a mixture of stereoisomers, as well as a lower limit of two. If the claim is going to recite, or imply that there are at least two stereoisomers, applicants will have to point to a page and line number in the specification where support may be found. Note that even if page 21 had recited that the "isomeric purity" of each isomer were 96% (rather than 99-6%), this would not support the lower limit of two stereoisomers, or for that matter two isomers.

\*

Claims 35-51 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Each of claims 35 and 42 recites "a mixture of stereoisomers consisting of two or more compounds of [the indicated structure]". However, this constitutes an ambiguity, since there is no requirement that the two (or more) compounds are stereoisomers of one another. The following could be used:

*A mixture consisting of a compound of the following structure, and at least one stereoisomer thereof.*

- Each of claims 35 and 42 recites (last line) "DPIV". There should be a hyphen

DPIV

However, this renders the claims indefinite as to whether the hydrolysis occurs at all.

Something more affirmative, such as the following, should be used:

*...a group which is hydrolyzed to...*

\*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 35-51 are rejected under 35 U.S.C. §103 as being unpatentable over Bachovchin (*J. Biol. Chem.* **265**, 3738, 1990) or Bachovchin (USP 4,935,493) or Bachovchin (WO 89/03223) or Flentke (*Proc Natl Acad Sci* **88**, 1556, 1991).

The teachings of the references were indicated previously. Applicants have argued that

particular argument will be left unchallenged. Applicants have further argued that *In re Wiggins* should provide applicants "immunity" from rejection based on Bachovchin (1990). While applicants may be correct that the particular passage on page 3743, col 1, paragraph 3 of Bachovkin (*J. Biol. Chem.* **265**, 3738, 1990) cannot be relied on, Wiggins does not bar the remaining teachings of the references from being used.

As it happens, the chemist of ordinary skill is aware that vastly better separations are obtained with HPLC using a gradient of increasing polarity (in the case of silica gel) than is the case if an isocratic gradient is used with a handpacked column using silica of much larger particle size. Thus, while it may be true that 100 passes through the latter column (handpacked, isocratic) will not be effective, notably absent is even an *assertion* that employing a gradient, and prep HPLC will be ineffective, even if silica is used. But the analysis need not end there. As it happens, C<sub>18</sub> is the single most commonly used HPLC column in existence. A chemist might choose to use this because of his own (positive) experience with it, or because his lab only has C<sub>18</sub> HPLC columns, and no silica HPLC columns. Perhaps the C<sub>18</sub> columns are less expensive than the silica HPLC columns; perhaps the C<sub>18</sub> columns last longer. There are any number of motivations. In addition, the claims encompass peptides of varying polarity. It would not take very many hydrophilic amino acids within substituent variable "X" or substituent variable A' to render

eluting solvent. Accordingly, a chemist of ordinary skill would have had motivation to use C<sub>18</sub>. If applicants believe that they are the first to discover the existence of C<sub>18</sub> columns, and would like to see references (published prior to April 14, 1990) discussing C<sub>18</sub> column chromatography, such references will be provided.

The rejections are maintained.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is (703) 308-3213.

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



DAVID LUKTON  
PATENT EXAMINER  
GROUP 1653